PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 29010-75970	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/32401	International filing date *(day/month/year)* 01 October 2004 (01.10.2004)	Priority date *(day/month/year)* 03 October 2003 (03.10.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07D 205/085, 201/08; A61K 31/397, 31/4178, 31/422, 31/4025 and US Cl.: 540/364, 363		
Applicant SERENIX PHARMACEUTICALS LLC		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 8 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____ , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02 August 2005 (02.08.2005)	22 December 2005 (22.12.2005)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Mark L. Berch J. Roberts for Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/32401

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into English, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4(a))

☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:
pages 1-74 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the claims:
pages NONE as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* 75-82 received by this Authority on 02 August 2005 (02.08.2005)
pages* NONE received by this Authority on _____

☐ the drawings:
pages NONE as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/32401

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims 1-28	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 26	YES
	Claims 1-25, 27 and 28	NO
Industrial Applicability (IA)	Claims 1-28	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)

Claims 1, 2, 10, 18-23, 25, 27-28 lack an inventive step under PCT Article 33(3) as being obvious over WO 97/30707. See Formula I on pages 3-4. Note example 161, corresponding to R4 = styryl, n=0, R1= H, A=OH, A' = t-butyloxy, (or vice versa), R3 = choice 1 with R10 as phenyl. Note also Example 162, corresponding to R4 = styryl, n=0, R1=H, A = triflouromethyl-benzylamino, A' = t-butyloxy, R3 = choice 1 with R10 as phenyl. The utility is the same. The claim 28 synthesis appear in the scheme on page 38. The sole difference is that applicants have an extra methyl group, R2 = methyl. Compounds that differ only by the presence or absence of an extra methyl group are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. See also MPEP 2144.09, second paragraph. The method claim 27 is included because there is no way of knowing which diseases are coved by the claim language.

Claims 1-25, 27-28 lack an inventive step under PCT Article 33(3) as being obvious over WO 03/031407. See Formula I on pages 2-3 and in particular, Formula III on page 16, and the species of Tables 1-15. These include mono-substituted amino choices (e.g. Table 2, next to last species) and disubstituted amino, e.g. Table 1, species 3. See also Scheme I on page 26 for the synthesis. The sole difference is that applicants have an extra methyl group, R2 = methyl. Compounds that differ only by the presence or absence of an extra methyl group are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. See also MPEP 2144.09, second paragraph.

The traverse is unpersuasive of these two rejections. Applicants argue that sticking on a methyl groups is not a homolog. There is no legal basis for such an assertion. First, homologs, the replacement of a H attached to a C with a methyl group, have long been accepted as evidence of close structural similarity in many, many cases. Applicants quote MPEP 2144.09 as saying "e.g., by -CH2- groups." First, the "e.g." indicates that this is just an example. And second, insertion of -CH2- into the preexisting C-H bond at the 3-position of the azetidinone ring with give this group. Applicants then discuss "isomers" but this is not an isomer situation and cite *Grabiak*, but that was O vs. S, again, not this situation. Applicants argue that adding the methyl provides "more steric hindrance" but that is true in all cases of homology, e.g. going from methyl to ethyl also provides more steric hindrance. Likewise, applicants argue that the methyl is not electronically equivalent to H. However, ethyl is not electronically equivalent to methyl either.

Claims 1-28 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/32401

Box No. VIII Certain observations on the international application

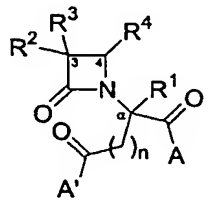
The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 27 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 27 is indefinite for the following reason(s): There is no way of knowing what the scope of this claim is. The V1a receptor is widely distributed in the body and appears in such diverse places as vascular smooth muscle, myometrium, the bladder, blood platelets, brain (in the prefrontal, cingulate, pyriform, and entorhinal cortex, as well as the presubiculum and mamillary bodies), kidney, reproductive organs, etc. It stimulates phospholipase A2, phospholipase C, and phospholipase D, PKC, PI3-induced Ca2+ release from the endoplasmic reticulum, can cuppress cAMP and has many other effects as well.

Claim 27 objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claim 27 not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: As noted above, this could have a staggering range of diseases being treated. No one compound — let alone a genus of billions, can do such a thing.

WHAT IS CLAIMED IS:

1. A compound of the formula



wherein:

n is an integer selected from 0, 1, and 2;

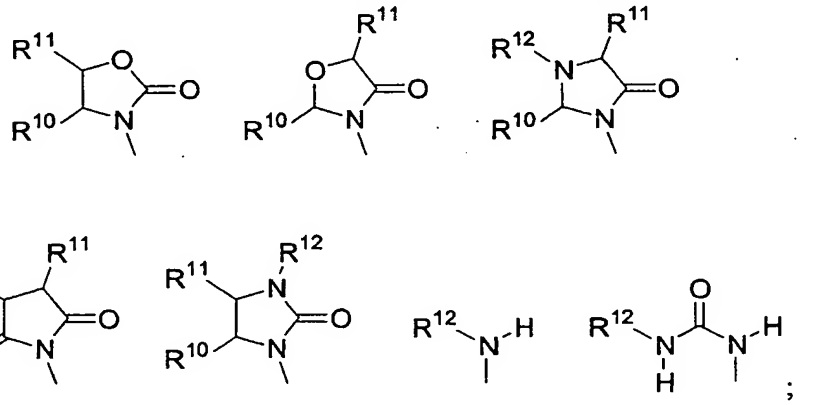
A is R^5O-, XNH-, or $R^{14}XN$-;

A′ is $R^{5'}O$-, X′NH-, or $R^{14'}X'N$-;

R^1 is hydrogen or C_1-C_6 alkyl;

R^2 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_4 alkoxy, C_1-C_4 alkylthio, halo, haloalkyl, cyano, formyl, alkylcarbonyl, alkoxycarbonyl, or a substituent selected from the group consisting of $-CO_2R^8$, $-CONR^8R^{8'}$, and $-NR^8(COR^9)$;

R^3 is a structure selected from the group consisting of



;

R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, C_3-C_9 cycloalkenyl, C_1-C_3 alkylcarbonyl, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_2-C_4 alkenyl), or optionally substituted aryl(C_2-C_4 alkynyl);

R^5 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkoxy)-(C_1-C_4 alkyl), optionally substituted aryl(C_1-C_4 alkyl), Y-, Y-(C_1-C_4 alkyl), and R^6R^7N-(C_2-C_4 alkyl);

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R^5 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkoxy)-(C_1-C_4 alkyl), optionally substituted aryl(C_1-C_4 alkyl), Y'-, Y'-(C_1-C_4 alkyl), and $R^{6'}R^{7'}N$-(C_2-C_4 alkyl);

Y and Y' are each independently selected from the group consisting of tetrahydrofuryl, morpholinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, and quinuclidinyl; where said morpholinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, or quinuclidinyl is optionally N-substituted with C_1-C_4 alkyl or optionally substituted aryl(C_1-C_4 alkyl);

X is selected from the group consisting of C_1-C_6 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkoxy)-(C_1-C_4 alkyl), optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_3-C_7 cycloalkyl), optionally substituted indan-1-yl, optionally substituted indan-2-yl, optionally substituted 1,2,3,4-tetrahydronaphth-1-yl, optionally substituted 1,2,3,4-tetrahydronaphth-2-yl, Y, Y-(C_1-C_4 alkyl), R^6R^7N-, and R^6R^7N-(C_2-C_4 alkyl);

R^{14} is selected from the group consisting of hydroxy, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, and benzyl; or

R^{14} and X are taken together with the attached nitrogen atom to form an optionally substituted first heterocycle, where said first heterocycle is selected from the group consisting of pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, pyrrolidinonyl, piperidinonyl, 2-(pyrrolidin-1-ylmethyl)pyrrolidin-1-yl, and 1,2,3,4-tetrahydroisoquinolin-2-yl;

X' is selected from the group consisting of C_1-C_6 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkoxy)-(C_1-C_4 alkyl), optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_3-C_7 cycloalkyl), optionally substituted indan-1-yl, optionally substituted indan-2-yl, optionally substituted 1,2,3,4-tetrahydronaphth-1-yl, optionally substituted 1,2,3,4-tetrahydronaphth-2-yl, Y', Y'-(C_1-C_4 alkyl), $R^{6'}R^{7'}N$-, and $R^{6'}R^{7'}N$-(C_2-C_4 alkyl);

$R^{14'}$ is selected from the group consisting of hydroxy, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, and benzyl; or

$R^{14'}$ and X' are taken together with the attached nitrogen atom to form an optionally substituted second heterocycle, where said second heterocycle is selected from the group consisting of pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl,

pyrrolidinonyl, piperidinonyl, 2-(pyrrolidin-1-ylmethyl)pyrrolidin-1-yl, and 1,2,3,4-tetrahydroisoquinolin-2-yl;

R^6 is hydrogen or C_1-C_6 alkyl; and R^7 is C_1-C_6 alkyl, C_3-C_8 cycloalkyl, optionally substituted aryl, or optionally substituted aryl(C_1-C_4 alkyl); or

R^6 and R^7 are taken together with the attached nitrogen atom to form an heterocycle selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, and homopiperazinyl; where said piperazinyl or homopiperazinyl is optionally N-substitued with R^{13};

$R^{6'}$ is hydrogen or C_1-C_6 alkyl; and $R^{7'}$ is C_1-C_6 alkyl, C_3-C_8 cycloalkyl, optionally substituted aryl, or optionally substituted aryl(C_1-C_4 alkyl); or

$R^{6'}$ and $R^{7'}$ are taken together with the attached nitrogen atom to form an heterocycle selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, and homopiperazinyl; where said piperazinyl or homopiperazinyl is optionally N-substituted with $R^{13'}$;

R^8 and $R^{8'}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, optionally substituted aryl, and optionally substituted aryl(C_1-C_4 alkyl); or

R^8 and $R^{8'}$ are taken together with the attached nitrogen atom to form an heterocycle selected from the group consisting of optionally substituted pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, and homopiperazinyl;

R^9 is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkoxy)-(C_1-C_4 alkyl), optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted heteroaryl, optionally substituted heteroaryl(C_1-C_4 alkyl), and $R^8R^{8'}N$-(C_1-C_4 alkyl);

R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_3-C_8 cycloalkyl, C_1-C_4 alkoxycarbonyl, C_1-C_5 alkylcarbonyloxy, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_1-C_4 alkyloxy), optionally substituted aryl(C_1-C_4 alkylcarbonyloxy), diphenylmethoxy, and triphenylmethoxy;

R^{12}, R^{13}, and $R^{13'}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_4 alkoxycarbonyl, optionally substituted

aryloxycarbonyl, optionally substituted aryl(C_1-C_4 alkyl), and optionally substituted aryloyl; and

hydrates, solvates, and pharmaceutically acceptable salts thereof.

2. The compound of claim 1, wherein A is XNH-.

3. The compound of claim 1, wherein A is $R^{14}XN$-.

4. The compound of claim 3, wherein R^{14} is selected from the group consisting of hydroxy, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, and benzyl; and where X is selected from the group consisting of C_1-C_6 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkoxy)-(C_1-C_4 alkyl), optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_3-C_7 cycloalkyl), optionally substituted indan-1-yl, optionally substituted indan-2-yl, optionally substituted 1,2,3,4-tetrahydronaphth-1-yl, optionally substituted 1,2,3,4-tetrahydronaphth-2-yl, Y, Y-(C_1-C_4 alkyl), R^6R^7N-, and R^6R^7N-(C_2-C_4 alkyl).

5. The compound of claim 3, wherein R^{14} and X are taken together with the attached nitrogen atom to form an optionally substituted first heterocycle.

6. The compound of claim 3, wherein R^{14} and X are taken together with the attached nitrogen atom to form an optionally substituted first heterocycle substituted with a substituent selected from the group consisting of optionally substituted C_1-C_6 alkyl, optionally substituted C_3-C_8 cycloalkyl, C_1-C_4 alkoxycarbonyl, C_1-C_5 alkylcarbonyloxy, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_1-C_4 alkyloxy), optionally substituted aryl(C_1-C_4 alkylcarbonyloxy), R^6R^7N-, and R^6R^7N-(C_1-C_4 alkyl).

7. The compound of claim 3, wherein R^{14} and X are taken together with the attached nitrogen atom to form a piperidinyl optionally substituted at the 4-position with hydroxy, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_4 alkoxy, (C_1-C_4 alkoxy)carbonyl, (hydroxy(C_2-C_4 alkyloxy))-(C_2-C_4 alkyl), R^6R^7N-, R^6R^7N-(C_1-C_4 alkyl), diphenylmethyl, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), or piperidin-1-yl(C_1-C_4 alkyl).

8. The compound of claim 3, wherein R^{14} and X are taken together with the attached nitrogen atom to form a piperazinyl optionally substituted at the 4-position with C_1-C_6 alkyl, C_3-C_8 cycloalkyl, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), α-methylbenzyl, N-(C_1-C_5 alkyl) acetamid-2-yl, N-(C_3-C_8 cycloalkyl) acetamid-2-yl, R^6R^7N-, or (C_1-C_4 alkoxy)carbonyl.

9. The compound of claim 3, wherein R^{14} and X are taken together with the attached nitrogen atom to form a homopiperazinyl optionally substituted in the 4-position with C_1-C_4 alkyl, aryl, or aryl(C_1-C_4 alkyl).

10. The compound of claim 1, wherein A′ is XNH-.

11. The compound of claim 1, wherein A′ is R^{14}XN-.

12. The compound of claim 11, wherein $R^{14'}$ is selected from the group consisting of hydroxy, C_1-C_6 alkyl, C_1-C_4 alkoxycarbonyl, and benzyl; and where X′ is selected from the group consisting of C_1-C_6 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 alkoxy)-(C_1-C_4 alkyl), optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_3-C_7 cycloalkyl), optionally substituted indan-1-yl, optionally substituted indan-2-yl, optionally substituted 1,2,3,4-tetrahydronaphth-1-yl, optionally substituted 1,2,3,4-tetrahydronaphth-2-yl, Y′, Y′-(C_1-C_4 alkyl), $R^{6'}R^{7'}N$-, and $R^{6'}R^{7'}N$-(C_2-C_4 alkyl).

13. The compound of claim 11, wherein $R^{14'}$ and X′ are taken together with the attached nitrogen atom to form an optionally substituted second heterocycle.

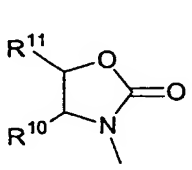
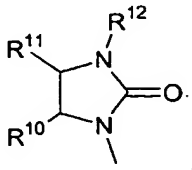
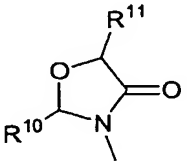
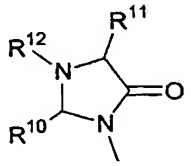
14. The compound of claim 11, wherein $R^{14'}$ and X′ are taken together with the attached nitrogen atom to form an optionally substituted second heterocycle substituted with a substituent selected from the group consisting of optionally substituted C_1-C_6 alkyl, optionally substituted C_3-C_8 cycloalkyl, C_1-C_4 alkoxycarbonyl, C_1-C_5 alkylcarbonyloxy, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_1-C_4 alkyloxy), optionally substituted aryl(C_1-C_4 alkylcarbonyloxy), $R^{6'}R^{7'}N$-, and $R^{6'}R^{7'}N$-(C_1-C_4 alkyl).

15. The compound of claim 11, wherein $R^{14'}$ and X′ are taken together with the attached nitrogen atom to form a piperidinyl optionally substituted at the 4-position with hydroxy, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_4 alkoxy, (C_1-C_4 alkoxy)carbonyl, (hydroxy(C_2-C_4 alkyloxy))-(C_2-C_4 alkyl), $R^{6'}R^{7'}N$-, $R^{6'}R^{7'}N$-(C_1-C_4 alkyl), diphenylmethyl, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), or piperidin-1-yl(C_1-C_4 alkyl).

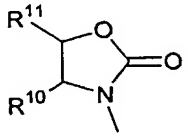
16. The compound of claim 11, wherein $R^{14'}$ and X′ are taken together with the attached nitrogen atom to form a piperazinyl optionally substituted at the 4-position with C_1-C_6 alkyl, C_3-C_8 cycloalkyl, optionally substituted aryl, optionally substituted aryl(C_1-C_4 alkyl), α-methylbenzyl, N-(C_1-C_5 alkyl) acetamid-2-yl, N-(C_3-C_8 cycloalkyl) acetamid-2-yl, $R^{6'}R^{7'}N$-, or (C_1-C_4 alkoxy)carbonyl.

17. The compound of claim 11, wherein $R^{14'}$ and X' are taken together with the attached nitrogen atom to form a homopiperazinyl optionally substituted in the 4-position with C_1-C_4 alkyl, aryl, or aryl(C_1-C_4 alkyl).

18. The compound of claim 1, wherein R^3 is a structure selected from the group consisting of

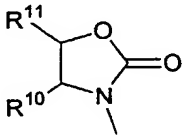
19. The compound of claim 1, wherein R^3 is



20. The compound of claim 1, wherein R^4 is optionally substituted aryl(C_1-C_4 alkyl), optionally substituted aryl(C_2-C_4 alkenyl), or optionally substituted aryl(C_2-C_4 alkynyl).

21. The compound of claim 1, wherein R^4 is optionally substituted aryl(C_2-C_4 alkenyl).

22. The compound of claim 1, wherein R^3 is


; and

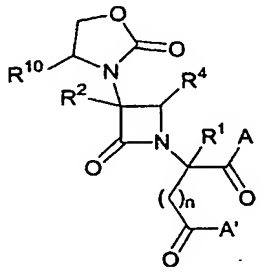
R^{10} is optionally substituted phenyl.

23. The compound of claim 18, wherein A is XNH-, where X is optionally substituted aryl(C_1-C_4 alkyl).

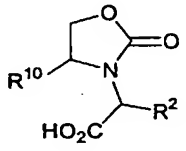
24. The compound of claim 18, wherein A′ is $R^{14'}XN$-, where $R^{14'}$ and X′ are taken together with the attached nitrogen atom to form an optionally substituted second heterocycle, said optionally second heterocycle selected from the group consisting of piperidinyl and piperazinyl.

25. A pharmaceutical composition comprising the compound of any of the preceding claims, where the compound is present in a pharmaceutically effective amount for treating a disease state responsive to antagonism of a vasopressin V_{1a} receptor in a mammal in need of such treatment; and a pharmaceutically acceptable carrier, diluent, or excipient.

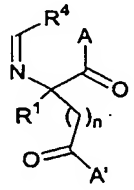
26. A process for preparing a compound of the formula:



wherein R^1, R^2, R^4, n, A, and A′ are as defined in claim 1, and R^{10} is optionally substituted aryl, the process comprising the step of reacting a compound of the formula:



with a compound of the formula:



27. A method for treating a disease state responsive to antagonism of a vasopressin V_{1a} receptor in a mammal in need of such treatment, the method comprising the step of administering to the mammal a pharmaceutically effective amount of the compound of any one of claims 1-24.

28. The method of claim 27, wherein the compound is included in a pharmaceutical composition comprising the compound and a pharmaceutically acceptable carrier, diluent, or excipient.